The information provided herein is considered JRD, LLC trade secrets, commercial or financial information that JRD, LLC customarily holds close and treats as confidential. The information is being provided under the assurance that the U.S. Department of Health and Human Services and all of its agencies, including the Assistant Secretary for Preparedness and Response, Biomedical Advanced Research and Development Authority, will maintain the confidentiality of the information under the Trade Secrets Act, Procurement Integrity Act, other applicable statutes, regulations, rules, case law contractual provisions, protective orders or otherwise and as such, the information provided herein is exempt from disclosure under Exemption 4 of the Freedom of Information Act ("FOIA").

AMENDMENT OF OTHER TRANSACTION AGREEMENT (OTA)

OTHER TRANSACTION FOR ADVANCED RESEARCH (OTAR)

Agreement Number HHSO100201700018C
Effective Date of Agreement: August 15, 2017

BETWEEN

JANSSEN RESEARCH & DEVELOPMENT LLC
920 ROUTE 202
RARITAN, NJ 08869, USA

AND

THE UNITED STATES OF AMERICA
DEPARTMENT OF HEALTH AND HUMAN SERVICES
BIOMEDICAL ADVANCED RESEARCH AND DEVELOPMENT AUTHORITY
O'NEILL HOUSE OFFICE BUILDING
WASHINGTON, DC 20515

CONCERNING

INFLUENZA PORTFOLIO AND OTHER EMERGING PATHOGENS DEVELOPMENT CANDIDATES

Amendment No. 0010

Amendment No. 0010 to the agreement updates the budget information and scope of work for various work packages that are related to COVID-19 vaccine research and development efforts. Because Amendment No. 0009 served primarily as a tool for administrative internal alignment, the new information provided in this document relate most closely to Amendment No. 0008. As such, the financial data provided in this amendment effectively serves as a budget update to Amendment No. 0008 of the agreement. All increases noted below reflect updates to Amendment No. 0008.

Effective Date of Modification: Upon Last Signature in Section III

Total Amount of the Agreement increased by (b) (4) for additional studies and activities in pre-clinical, Phase I & Phase II related to the COVID-19 vaccine (including government and

recipient funding). The total amount of the agreement for all assets in the OTA is raised from (b) (4) to (b) (4)

Government Share of Total Amount of the Agreement is increased by $85,304,775 from $1,019,201,353 to $1,104,506,128.

Recipient Share of Total Amount of the Agreement is increased by (b) (4) from (b) (4) to (b) (4)

Current Government commitment: With additional studies (i.e. Work Package [WP] 6.2 and WP 6.17) and other adjustments to WP 6.1 - 6.10 and 6.13 - 6.17, the total, obligated governmental funds obligated is increased by $85,304,775 from $689,525,867 to $774,830,641.

Current Recipient commitment: The obligated recipient funds provided in Mod 0008 is decreased by (b) (4) With additional studies (WPs 6.2 and 6.17) and other adjustments to WP 6.1 - 6.10 and 6.13 - 6.17, the total, obligated recipient funds is increased by (b) (4) from (b) (4) to (b) (4)

Period of Performance: The Period of Performance of this agreement is extended from December 31, 2024 to December 31, 2025.

Authority: Section 319L(C)(5) of the Public Health Service Act, 42 USC 247d-7e(C)(5).

Line of Accounting and Appropriation:

Work Packages	Title	Requisition (OS)	CAN	Obj.Class	Amt. (Govt Share)	Changed
(b) (4)						
WP 6.1 – 6.10, and 6.13 – 6.17	COVID-19 - Vaccines discovery thru Phase 3 Trial, excluding WPs 6.11 and 6.12.	OS256464 OS262675	199COV1 199C014	25103 25103	$456,237,081 $85,304,775 $541,541,855	Adjusted with this modification
(b) (4)						
Total					$774,830,641	**Changed**

I. AMENDMENT PURPOSE

This Amendment, based on Joint Oversight Committee (JOC) recommendation, documented in Memo #12 dated 16 June 2020, and in accordance with Article IV of the OTA, adds (i) a non-human primate (NHP) within Work Package (WP) 6.2, (ii) adds a Randomized, Double-blind, Placebo-controlled Phase 2 study (WP 6.17), and (iii) revises work packages (prior to Phase 3).For the purposes of this SOW update, the work packages associated with the Phase 3 Study (WPs 6.10 – 6.13) have been marked as RESERVED as they are in the process of being updated , and these changes will be reflected in a forthcoming Amendment. All changes to cost are captured in

This Amendment also clarifies the terminology used to describe the subcontractor notification process described in Article XIII "Subcontracting". The process in which notification is provided to BARDA shall be referred to as the "Contracting Officer Notification (CON)" process.

By the Parties' mutual agreement and within the existing Agreement's general scope, to include specific terms and conditions applicable to COVID related activities as described in Amendments 0007 and 0008, this Amendment No. 0010 bilaterally:

i. Incorporates the updated budget;
ii. incorporates the updated Statement of Work (Exhibit A);
iii. Adds language to Article XIII Subcontracting, to clarify Contracting Officer Notification terminology;
iv. In Article XIII Subcontracting, replace "calendar day" with "business day";
v. In Article XIII Subcontracting, replace references to Amendments 0007 & 0008 with "COVID-19 Antiviral and Vaccines efforts"
vi. Adds language defining a "Publications" and "Presentations;"
vii. Adds language requiring acknowledgement of federal funding; and
viii. Closes out the "redirect" of funding from NOI JOC #12, dated June 18, 2020

II. AMENDMENTS TO AGREEMENT

A. Incorporate new Cost Share Estimates/Budget Summary in accordance with the updated budget.

1) Pursuant to Agreement Article VI(C), the budget allocation summary of assets is hereby replaced to incorporate **Table 1 – Cost Share Estimates Budget Summary***.

(b) (4)

[redacted]

Updated the Statement of Work - The Statement of Work shall be replaced to reflect the changes in WPs 6.1-6.10 and 6.14-6.17. For purposes of this updated SOW, work packages associated with the Phase 3 Study (WPs 6.10 – 6.13) have been marked as RESERVED as they are in the process of being updated and will be restated in a forthcoming Amendment. The updated SOW (other than Phase 3) for incorporation in the OTA is included in **Exhibit A**. The corresponding WP budget **Table 2 - Budget Allocation Summary)**, with shaded options in gray, replaces all previous budget work package tables.

C. Article XIII: Add the following language to the end of the first paragraph of the Article: "For clarity and consistency, the review period for subcontracts planned within the scope of the OTA shall be referred to as the Contracting Officer Notification (CON) or Other Transaction Agreement Officer Notification (OTAON) process."

ARTICLE XIII SUBCONTRACTING, incorporating changes iii-v from Amendment Purpose, shall now be replaced with the following:

For any subcontracts in excess of (b) (4) that will be reimbursed under this Agreement, Recipient will provide BARDA the opportunity to review the subject subcontracting agreement seven (7) business days before execution. The subcontract agreement shall include the nature of the work that the subcontractor is going to perform, an estimated period of performance and the proposed costs for the work. Recipient will provide OTTR, OTAO, OTAS and OTTS with an electronic copy of the subcontracting document. For avoidance of doubt, the Recipient is not required to wait for the Government's comments before executing an Agreement with a subcontractor once the 7-business day review period has expired. For clarity and consistency, the review period for subcontracts planned within the scope of the OTA shall be referred to as the Contracting Officer Notification (CON) or Other Transaction Agreement Officer Notification (OTAON) process."

For this COVID-19 Antiviral and Vaccines efforts only, for any subcontracts in excess of (b) (4) that will be reimbursed under the OTA, Recipient will provide BARDA the opportunity to review the subject subcontracting agreement three (3) business days before execution. The subcontract agreement shall include the nature of the work that the subcontractor is going to perform, an estimated period of performance and the proposed costs of the work. Recipient will provide OTTR, OTAO and OTTS with an electronic copy of the subcontracting document. For avoidance of doubt, the Recipient is not required to wait for the Government's comments before executing an Agreement with a subcontractor once the 3-business day review period has expired.

D. The following Articles and language are added to the agreement:

ARTICLE XVII: PUBLICATIONS AND PRESENTATIONS

Publications

Publications shall mean written scientific meeting abstract(s), scientific journal article(s) or other articles authored or co-authored by Recipient's personnel or Recipient's subcontractor personnel containing data generated under this OTA.

Any scientific meeting abstract, scientific journal article, or other articles, authored or co-authored by any Recipient personnel or Recipient's subcontractor personnel, which contains data generated under Biomedical Advanced Research and Development Authority ("BARDA"), OTA No. HHSO100201700018C must be submitted to the OTAR for review no less than 30 calendar days prior to submission for publication. However, the Parties may agree to negotiate abbreviated timeframes, as needed.

Presentations

Any Presentation materials containing data generated under this OTA, authored/co-authored or to be delivered by or on behalf of, any Recipient or Recipient's vendor's personnel, must be submitted to the OTAR for review no less than 15 calendar days prior to the presentation. However, the Parties may agree to negotiate abbreviated timeframes, as needed.

Presentations shall mean any materials containing data generated under this OTA, authored, co-authored, or to be delivered by or on behalf of, any Recipient or Recipient's vendor's personnel.

ARTICLE XVIII: ACKNOWLEDGEMENT OF FEDERAL FUNDING in MEDIA and PRESS RELEASES

The Recipient shall accurately and factually represent the work conducted or to be conducted under the OTA. The Recipient shall acknowledge the support of the Department of Health and Human Services, Office of the Assistant Secretary for Preparedness and Response, Biomedical Advanced Research and Development Authority whenever publicizing the work under this OTA in any media by including an acknowledgment substantially as follows:

"This project has been funded in whole or in part with Federal funds from the Office of the Assistant Secretary for Preparedness and Response, Biomedical Advanced Research and Development Authority, under OTA No. HHSO100201700018C."

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Except as provided in this Amendment, all terms and conditions of the Agreement, unless previously changed, remain unchanged and in full force and effect.

III. SIGNATURES

Acknowledged, accepted, and agreed for

Janssen Research & Development, LLC

(b) (6)

DATE:

U.S. Department of Health & Human Services
Office of the Assistant Secretary for
Preparedness & Response

(b) (6)

DATE: 8.27.2020

Table 1 – Cost Share Estimates Budget Summary

M0010 Cost Share Estimates/Budget Summary									
Summary	Invoiced 8/15/2017 Through 12/31/2018	1/1/2019 Through 12/31/2019	1/1/2020 Through 12/31/2020	1/1/2021 Through 12/31/2021	1/1/2022 Through 12/31/2022	1/1/2023 Through 12/31/2023	1/1/2024 Through 12/31/2024	1/1/2025 Through 12/31/2025	Total
(b) (4) (BARDA:Janssen) Cost Share		Period 1	Period 2	Period 3	Period 4	Period 5	Period 6	Period 7	
[redacted]									
(b) (4) (BARDA:Janssen) Cost Share									
Funded -COVID-19 Vaccines discovery - Phase 3 Clinical Trial	(b) (4)								
[redacted]									
TOTAL including Options	(b) (4)								
BARDA funding									
Janssen funding									
Total Program									
BARDA funding									
Janssen funding									

Table 2 - Budget Allocation Summary

M0010 Exhibit B - Budget Allocation Summary									
		1/1/2019 through 12/31/2019	1/1/2020 through 12/31/2020	1/1/2021 through 12/31/2021	1/1/2022 through 12/31/2022	1/1/2023 through 12/31/2023	1/1/2024 through 12/31/2024	1/1/2025 through 12/31/2025	Cost Estimate 100%
Work Package Number	Work Package Name	PERIOD 1	PERIOD 2	PERIOD 3	PERIOD 4	PERIOD 5	PERIOD 6	PERIOD 7	TOTAL
(b) (4)									
WP 6.1	WP 6.1 (CLIN 0001) Antigen design, manufacturability testing and preMV5 manufacturing								
WP 6.2	WP 6.2 (CLIN 0002) Pre-Clinical Immunology								
WP 6.3	WP 6.3 (CLIN 0003) CMC Development until First in Human ("FIH")								
WP 6.4	WP 6.4 (CLIN 0004) Clinical Development and Regulatory Activities to Start First In Human Study								
WP 6.5	WP 6.5 (CLIN 0005) GLP Toxicology								
WP 6.6	WP 6.6 (CLIN 0006) GMP Manufacturing to Enable Clinical Trials								
WP 6.7	WP 6.7 (CLIN 0007) Phase 1/2a Clinical Trial								
WP 6.8	WP 6.8 (CLIN 0008) CMC Development and GMP Manufacturing Process to Enable Large Scale Manufacturing and Launch to Support the Regulatory Filing								
WP 6.9	WP 6.9 (CLIN 0009) Toxicology Studies								
WP 6.10	WP 6.10 (CLIN 0010) Phase 3 Study Adults								
WP 6.13	WP 6.13 (CLIN 0013) Other Clinical Studies								
WP 6.14	WP 6.14 (CLIN 0014) Regulatory Support								
WP 6.15	WP 6.15 (CLIN 0015) Project Management Support								
WP 6.16	WP 6.16 (CLIN 0016) Dissecting the Evolution of SARS-CoV-2 and Specific Humoral and Cellular Immunity Following Infection								
WP 6.17	WP 6.17 (CLIN 0017) Phase 2 Study								
	SUBTOTAL								
WP 6.11	OPTION - WP 6.11 (CLIN 0011) Pediatric Study								
WP 6.12	OPTION - WP 6.12 (CLIN 0012) High-risk Populations								
	SUBTOTAL of OPTIONS								
	TOTAL including OPTIONS								

(b) (4)

(b) (4)

July 1, 2020

COVID-19 Vaccine SoW

In response to the COVID-19 outbreak, Janssen has mobilized many resources to develop a vaccine based on its AdVac® and PER.C6® platform within an unprecedented short time frame. Vectors based on Adenovirus serotype 26 (Ad26) with different designs of the SARS-CoV-2 spike (S) protein have been tested for their suitability as a vaccine candidate in terms of manufacturability and immunogenicity in different animal species. A lead vaccine candidate has been selected, and the first steps of GMP manufacturing have started. Drug Product will be available for assessment of safety, tolerability and immunogenicity in humans in a Phase 1/2a clinical study in July 2020.

Given the emergency with the current COVID-19 outbreak, several activities have started in parallel to minimize white space between the activities and different phases of the project. With the exception of WPs 6.11 to 6.13, activities in all WPs have started. WP6.17, which defines a dose- and regimen-finding study, has been added in this version of the SoW.

Janssen is working closely together with the FDA and regulatory agencies in several other countries to discuss the plans both from a manufacturing and control strategy perspective as well as non-clinical safety and immunogenicity perspective.

Similar to the earlier versions of the SoW, the information provided herein reflects our best estimates based on the facts and circumstances as we know them today but could change as performance proceeds and more information becomes available. Additionally, due to the uncertainty of the spread, duration, and impact of the current COVID-19 outbreak, it is difficult to provide more precise estimates for the duration or cost for all of the activities contained in this proposal. As such, all activities, deliverables, milestones, and decision points described below may be subject to change in accordance with the governance process outlined in the OTA and relevant Amendments. In addition, associated timelines assume that business continuity at J&J and third parties will be sufficient to support the described activities.

WP6.1 Antigen design, manufacturability testing and preMVS manufacturing

Activities

- DNA encoding for several designs of the SARS-CoV-2 spike protein will be ordered at multiple CROs
- Research batches of Ad26 vectors with transgenes that encode for the different designs of the spike protein will be produced
- A small-scale manufacturability test will be done to determine platform fit of the different Ad26-based vaccine candidate expressing the different designs of the spike protein.

(b) (4)

- The PreMVS, with selected antigen, will be released based on the following assays:

(b) (4)

- Several critical reagents such as expression plasmids, soluble proteins, peptide pools and detection antibodies will be generated or ordered

Milestones

- Selection of Ad26-based COVID-19 vaccine candidate for start of preMVS manufacturing
- Transfer of preMVS to development organization
- Release of preMVS (Triggers WP6.7)

Deliverables

- (b) (4)
- PreMVS CoA
- PreMVS manufacturing report

Go/No go decisions

- Outcome of (b) (4) and immunogenicity assessment triggers a "go" for preMVS manufacturing and start of CMC method development and GMP manufacturing preparations
- Selection of Ad26-based COVID-19 vaccine candidate for start of preMVS manufacturing (Triggers WP6.6)

WP6.2 Pre-Clinical Immunology (Performed at Janssen or BIDMC)

Activities

- Mice, (b) (4) and non-human primates (NHP) will be immunized with DNA constructs of candidate vaccine inserts to set up immunogenicity assays and to get a first idea of immunogenicity.
- Ad26-based candidate vaccines will be tested for immunogenicity (b) (4) mouse (b) (4) Syrian hamster, rabbits, (b) (4) and NHP.

  - **June 2020 update:** Additional small animal immunogenicity studies in mice and Syrian hamster are planned with the selected lead candidate Ad26COVS1.
- Mice, Syrian hamster, rabbits, (b) (4) and NHP will be considered for viral challenge studies. If challenge models can be developed, animals from immunogenicity studies with Ad26-based vaccine candidates may be rolled over to a challenge study to determine preclinical vaccine efficacy.
  - **June 2020 update:** Additional viral challenge studies in Syrian hamster and NHP are planned to determine vaccine efficacy of lead candidate Ad26COVS1. The aim of these studies is to evaluate vaccine efficacy after different dose levels, compare one to two doses, evaluate durability of immune response and vaccine efficacy in older animals.

(b) (4) [redacted]

- Existence and relevance of vaccine-induced enhanced disease will be assessed in immunogenicity readouts in mice, and in viral challenge models in Syrian hamster and NHP. (b) (4) [redacted]

Milestones

- Initial PoC based on immunogenicity of DNA vaccine constructs
- PoC based on immunogenicity of Ad26-based vaccine candidates
- PoC based on protective efficacy of Ad26-based vaccine candidate in NHP

Deliverables

- Study reports of in vivo studies

Go/No go decisions

- Proof of immunogenicity triggers go for preMVS manufacturing
-

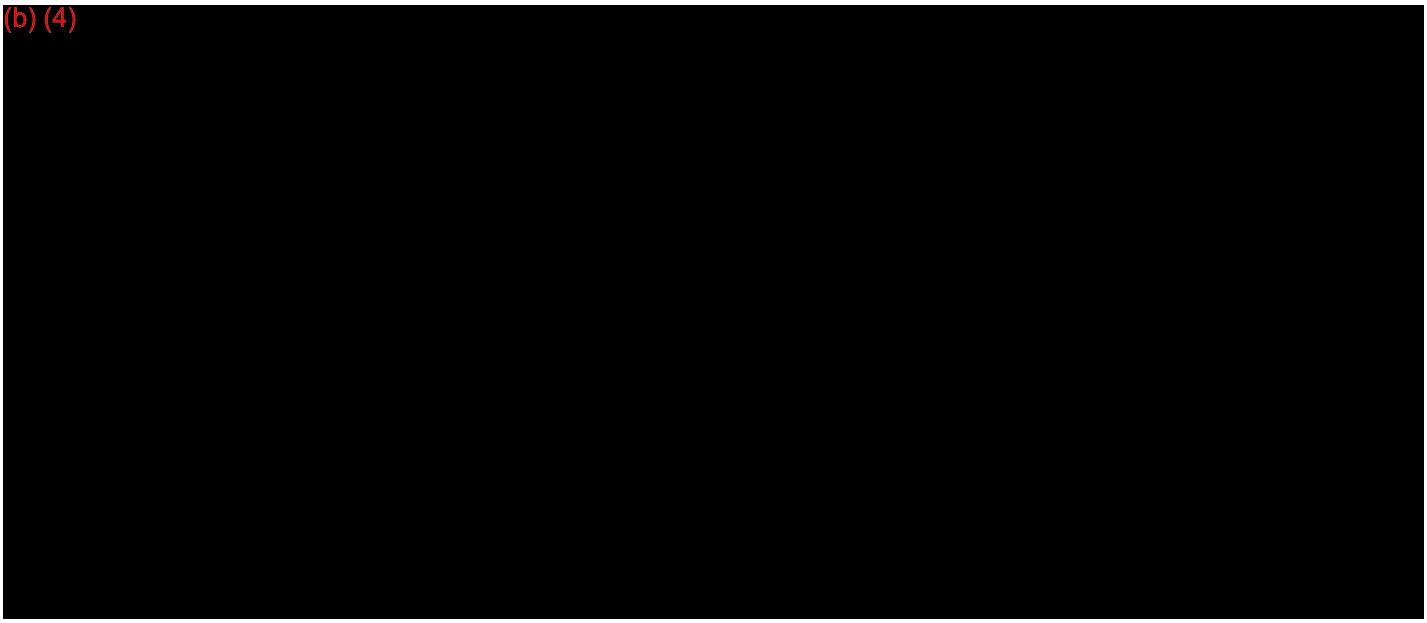
WP6.3 CMC Development until First in Human ("FIH")

Activities:

- Previously generated AdVac® platform data and prior experience will be leveraged as much as possible from a manufacturing development. To de-risk the R&D program we are planning to perform one or two DS development runs.

(b) (4) [redacted] method development will occur to make insert specific assays fit for purpose.

- (b) (4) [redacted]



WP6.4 Clinical Development and Regulatory Activities to Start First in Human Study

Activities

- Setup of immunological assays at CROs or at Janssen:
  - VNA, ELISA, ICS and ELISpot
- Writing of protocol elements document (PED)
- Protocol writing
- Writing and submission of preIND document
- Writing and submission of IND documents
- Contracting with vendors
- Contracting with clinical sites

Milestones

- PreIND meeting
- IND open

Deliverables

- Development reports assays
- PED
- Clinical Protocol
- preIND briefing book
- preIND minutes
- IND
- Investigators Brochure

Go/No go decisions

- IND submission triggers start clinical trial (WP6.7)

WP6.5 GLP Toxicology

Activities

- A GLP Toxicity study will be performed in rabbits.

(b) (4) [redacted]

WP6.6 GMP Manufacturing to Enable FIH Clinical Trial

- Master Virus Seed manufacturing and release
- Working Virus Seed manufacturing and release
- Multiple drug substance batches (b) will be manufactured (b) (4) [redacted]
- Drug Product manufacturing will happen (b) (4) [redacted]
- Packaging/labeling and distribution.
- Release and stability analysis will happen (b) (4) [redacted]
- (b) (4) [redacted]

(b) (4) [redacted]

(b) (4)

WP6.7 Phase 1/2a Clinical Trial

Activities

- A Randomized, Double-blind, Placebo-controlled Phase 1/2a Study to Evaluate the Safety, Reactogenicity, and Immunogenicity of Ad26COVS1 in Adults Aged 18 to 55 Years Inclusive and Adults Aged 65 Years and Older.
- Primary objective will be assessment of safety and reactogenicity. Secondary and exploratory endpoints will evaluate vaccine-induced immune responses to SARS-CoV-2.
- Two dose levels (high dose and low dose) given intramuscularly, will be evaluated, either as a single immunization, or as two immunization regimens, and compared to placebo
- Study cohorts:
    - Cohort 1:
        - Cohort 1a: 375 participants (75 participants per group) aged ≥18 to ≤55 years who will be randomized in parallel in a 1:1:1:1:1 ratio to 1 of 5 vaccination groups.
        - Cohort 1b: 25 participants (5 participants per group) aged ≥18 to ≤55 years who will be enrolled at the Beth Israel Deaconess Medical Center (BIDMC) and randomized in parallel in a 1:1:1:1:1 ratio to 1 of 5 vaccination groups. Additional exploratory immunogenicity evaluations (eg, epitope mapping, passive transfer, and certain analyses of functional and molecular antibody characteristics) will be performed for Cohort 1b.
    - Cohort 2: 270 participants aged ≥18 to ≤55 years will be randomized to receive Ad26COVS1 (240 participants) or a placebo (30 participants) in the regimens scheduled for the Phase 3 ie single immunization with 10e11 or two immunizations of 5x10e10 spaced 56 days apart. Cohort 2 will include an evaluation of a single booster vaccination given either at 6,12 or 24 months for each of the two regimens
    - Cohort 3: 375 participants (75 participants per group) aged ≥65 years who will be randomized in parallel in a 1:1:1:1:1 ratio to 1 of 5 vaccination groups.
- Total study size is targeted at 1.045 subjects
- Th1/Th2 determination to characterize immune response; this is relevant in light of the unproven, yet, theoretical possibility of enhanced respiratory disease (ERD) will be measured in approximately half of the subjects in cohorts 1 and 3.

- Serum and PBMC (PBMC in Cohorts 1 and 3, and a subset of Cohort 2) will be collected at day(s) of immunization, and at days 7, 14 and 28 after each immunization. Durability of immune responses will be measured at 6 months and after one year after last dose.
- Five subjects/group within Cohort 1 will be enrolled at BIDMC; samples will be subject to exploratory immune studies.
- Immuno sample analysis and long-term storage.

Milestones

- Safety analysis of solicited and unsolicited AEs after the 1st 15 subjects in Cohort 1
- Interim analysis Cohort 1 after first dose for Safety and Immunogenicity
- Interim analysis Cohort 3 after 1 dose
- Primary Analysis Cohort 1 after 2nd dose for Safety and Immunogenicity
- Final analysis top line results.

Deliverables

- TLR reports
- Clinical study report

Go/No go decisions

- Safety analysis of solicited and unsolicited AEs after the 1st 15 subjects in Cohort 1 in order to proceed to Cohort 3 and to proceed to Study COV2001.
- Interim analysis Cohort 1 after first dose for Safety and Immunogenicity to decide whether to proceed to a Phase 3 efficacy study in adults ≥18 to ≤59 years of age, and Cohort 2 in this study. This decision is based on adequate 28-day safety, immunologic responses including Neutralizing antibody and a TH1-like response indicating it will be safe and that the vaccine should induce protective responses. This in combination with appropriate preclinical studies.
- Interim analysis Cohort 3 after 1 dose as a Go/No go proceed to Phase 3 efficacy trial in participants aged ≥60 years.
- Primary analysis Cohort 1 after 2 doses for Safety and Immunogenicity to demonstrate the expected increased response in antibodies to justify the 2nd immunization in the 2-dose regimen in Phase 3.

WP6.8 CMC Development and GMP Manufacturing Process to Enable late phase clinical studies, Large Scale Manufacturing and Launch to Support the Regulatory Filing

(b) (4) [redacted]

- Drug Product manufacturing for later phase clinical use will happen (b) (4) [redacted]

(b) (4)

- It has become clear that a multidose presentation will be selected to fulfill the expected demand. (b) (4)
- The analytical methods will be validated (b) (4)
- PPQ for both DS and DP will be executed. (b) (4) (b) (4) .

(b) (4)

- Studies to enable launch and support licensure will be assessed and executed as appropriate.

(b) (4)

(b) (4) [redacted]

WP6.9 Toxicology Studies

A Phase 1 enabling GLP toxicology study is described under WP6.5. (b) (4) [redacted]

Activities

- Conduct developmental and reproductive toxicity (DART) study
  - This will be a combined embryo-fetal and pre- and postnatal development study, likely to be conducted in the rabbit.
  - (b) (4) such study would normally be conducted in parallel with Phase 3, (b) (4) [redacted]

Milestones / Deliverables

- DART study report completed

Go/No go decisions

- There are no Go/No go decision linked to the DART study.

WP6.14 Regulatory Support

Activities to establish an IND for an Ad26-based COVID-19 vaccine will involve an arrangement of a pre-IND meeting with CBER before the intended IND submission (b) (4) [redacted] Prior to the pre-IND, Janssen will discuss critical developmental aspects in Technical Working Group meeting(s) with FDA. Hence, throughout the program, RA CMC, Global Regulatory Affairs (RA) and regional RA support will be needed by preparing the respective working group meetings and providing regulatory advice internally within the Company.

As both pre-IND, IND and subsequent regulatory documentation will be supported by platform data both from a PER.C6® cell line perspective as the Ad26 vector, as well as use of non-clinical and clinical safety data from other developmental vaccines from Janssen, this platform information will need to be written down to be shared with the Agency. This activity will be coordinated by RA with support of the relevant CMC, non-clinical and clinical experts in the Company.

The pre-IND and IND preparation to enable Phase 1 will be led by RA. Further regulatory activities beyond Phase I are interactions with FDA to support the development of the vaccine up to regulatory submission (to be discussed: pre-EUA and/or BLA submission, or other pathways as per Agency's guidance). This involves an end-of-Phase 2 meeting and a pre-BLA meeting. Type C meetings will be scheduled on an as-needed basis. Pediatric requirements will be discussed as per Agency's requirements.

Annual reports will be prepared and submitted to CBER according to the foreseen timelines after the IND comes into effect. Development of regulatory intelligence with respect to development and licensing of a COVID-19 vaccine will carefully be monitored.

Discussions with other regulatory Agencies as required by the program and in particular to allow for a harmonized approach from a CMC, non-clinical and clinical development perspective, and facilitate multi-country trials as required per discussion with the Agencies, may also have to be conducted and will then be covered under WP6.14.

WP6.15 Project Management Support

This WP includes the Program Management activities associated with development of an Ad26-based COVID-19 vaccine. The program will have an Asset Project Management Leader (Asset PML) who will oversee their specific Project Management requirements. This includes conducting frequent and regular Project Management Team (PMT) meetings to ensure the accurate developing and tracking of the budget, timeline and resource plan. The Project Management team of each asset will also include relevant functional Project Managers and a Finance Representative. The Program will also have an Asset Technical Lead (CDT-L) who will oversee their specific Technical requirements. This includes conducting frequent and regular Compound Development Team (CDT) meetings to define the overall development strategy. The CDT of each asset will include, but is not limited to, the Technical Lead, Preclinical Leader, Clinical Leader, the

CMC Leader and, the Regulatory Leader. Clinical Team (CT) and Trial teams will oversee clinical program and trial execution. These teams include operational staff, Operational Leader and representatives of operational departments such as data management; GCO; medical writing, programming, stats. Additional expertise required for executing asset-specific work possibly including subcontractors may be added as part of PMT, CT and CDT.

WP6.16 Dissecting the Evolution of SARS-CoV-2 and Specific Humoral and Cellular Immunity Following Infection

Activities

- The understanding of the roles that polyclonal antibody responses to SARS-CoV-2 are thought to play in protection, disease resolution, or enhancement of disease are evolving with the assessment of patients with varying disease outcomes. The role of T cell responses is being investigated as well. Qualitative and quantitative characterization of immune responses upon SARS-Cov-2 infection, potentially in relation to outcome, could help to inform vaccine development.
- Identification of antigen-specific biomarkers of disease trajectory (survival, disease, death) and SARS-CoV-2 specific immune responses against the virus by (b) (4) approaches (b) (4) using samples from previously and prospectively collected, longitudinal cohorts at the (b) (4)

Milestones

- (b) (4)
- Biophysical characterization of antigen-specific antibody responses by Fc-receptor Luminex array and glycosylation profiling (S and RBD proteins of SARS-CoV2, SARS1, MERS, and other respiratory viruses; Galit Alter, Massachusetts General Hospital, Boston, MA)
- Functional characterization of antigen-specific antibody responses using antibody-dependent cellular phagocytosis (ADCP), complement deposition (ADCD), neutrophil or dendritic cell phagocytosis (ADNP and ADDCP), NK-cell activation and cytotoxicity (ADNA and ADCC), ERD, and other ADxx assays (SARS-CoV-2 S antigen; Galit Alter, Massachusetts General Hospital, Boston, MA)

Deliverables

- Study reports

Go/ no-go: There are no Go/No go decisions linked to these characterizations.

WP6.17 Phase 2 study - NEW

The phase 2 study VAC3158COV2001 will address a number of questions that will guide the dose and schedule selection for emergency use. In this study lower doses of Ad26COVS1 will be tested to determine if protective levels of VNA can be achieved with lower vaccine doses. A second goal is to see whether there will be a strong and rapid anamnestic response to SARS-CoV-2 infection after 1- and 2-dose regimens. Furthermore, a shorter and longer interval in the 2-dose regimen will be tested to gather insight on the possible compression and delay of the vaccination schedule, as this may be of interest in an emergency use setting.

This is a Randomized, Double-blind, Placebo-controlled Phase 2a Study to Evaluate a Range of Dose Levels and Vaccination Intervals of Ad26COVS1 in Healthy Adults Aged 18 to 55 Years Inclusive

In this study, safety and immunogenicity responses following 2-dose (5x10e10 vp, 2.5x10e10 vp, 1.25x10e10) and single-dose (5x10e10 vp and 1x10e11 vp) primary vaccination regimens will be assessed, to investigate dose sparing measures resulting in an increase of the number of vaccine doses available in a pandemic context. Safety and immunogenicity of 0,28-, 0,56-, and 0,84-day vaccination intervals for the 2-dose regimen (5x10e10 vp) will also be assessed.

A target of approximately 550 adult male and female participants will be enrolled in this study and will be randomly assigned to 1 of 10 groups.

Participants will receive Ad26COVS1 or a placebo intramuscularly. Four dose levels of Ad26COVS1 will be administered: 1×10e11 vp, 5×10e10 vp, 2.5x10e10 vp, and 1.25x10e10 vp.

Milestones

- An interim analysis of safety and immunogenicity will be performed, including 28-day immunogenicity (if applicable) and 28-day safety data post vaccination 1 of all groups
- The primary analysis of safety and immunogenicity post-vaccination 2 will be performed when all participants have completed the visit that takes place 28 days after the last study vaccination in all groups, or discontinued earlier
- A second interim analysis of safety and immunogenicity will be performed, including 28-day immunogenicity and 28-day safety data post antigen presentation of all groups
- The final analysis will be performed when all included participants have completed the last visit, or discontinued earlier

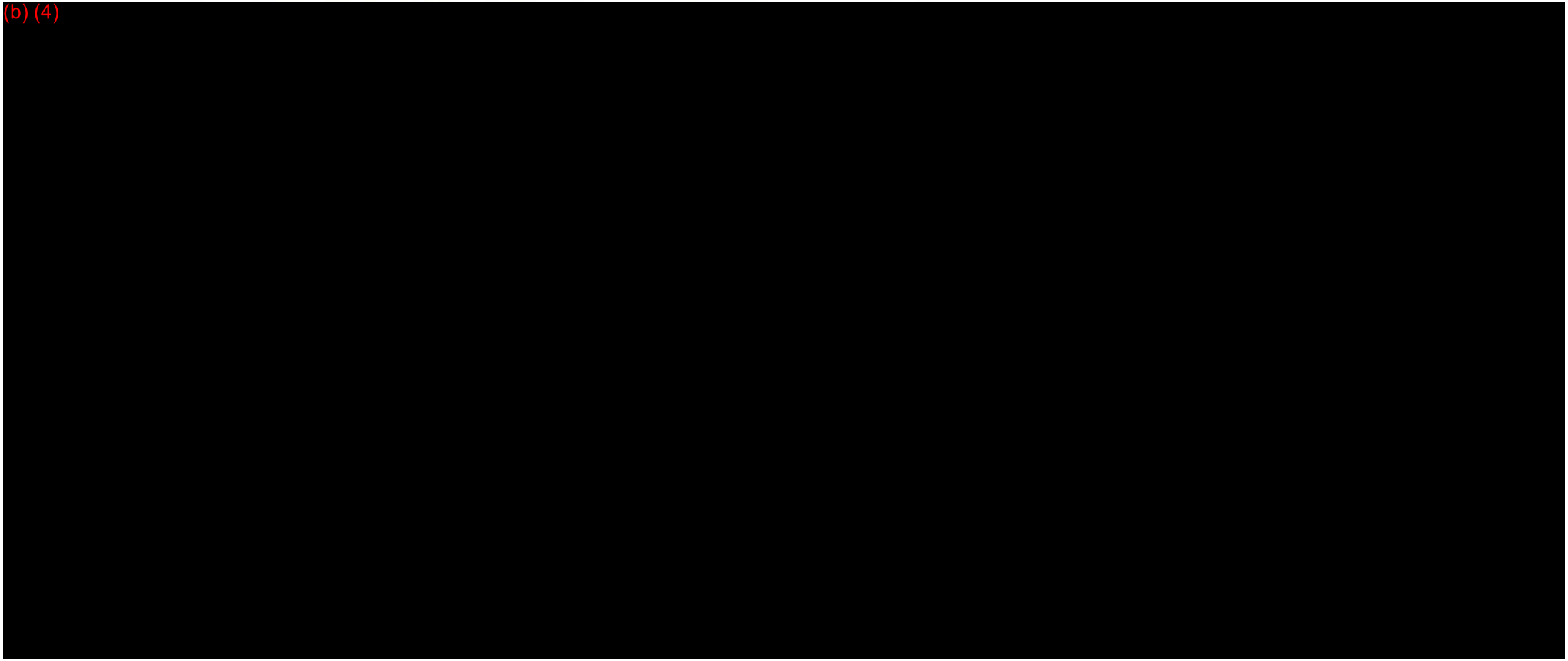
Deliverables

- TLR reports
- Clinical study report

Go/No go decisions

- Go-No go for inclusion of shorter regimen for emergency use
- Go-No Go for consideration of lower dose for Emergency use

(b) (4)



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